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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/694,758	10/23/2000	Shukti Chakravarti	CWV-001.01	7408

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EXAMINER

PONNALURI, PADMASHRI

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 02/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/694,758

Applicant(s)

CHAKRAVARTI, SHUKTI

Examiner

Padmashri Ponnaluri

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5-7 and 19-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5-7, 19-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/14/03 has been entered.
2. This application claims priority to provisional application 60/160,835, filed on 10/23/00.
3. Claims 5-7 and 19-29 are currently pending in this application.
4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
5. Claims 5-7 and 19-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claims briefly recite a method for determining an IBD or pre-IBD phenotype of a test cell, by detecting differential expression of at least five genes shown in table 1.

The specification description is directed to a method comprising I) generating a first library of nucleic acid probes representative of genes expressed by intestinal tissue of an animal without apparent risks or symptoms of IBD; ii) generating a second library of nucleic acid probes representative of genes expressed by intestinal tissue of animal which has symptoms of IBD;

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iii) identifying the genes up or down regulated, and use thus identified genes in the method of determining a phenotype of a cell. Thus genes involved in up or down regulated in **IBD condition have to be identified and probes of these genes are generated and formed micro arrays of the generated probes and the arrays in identifying phenotype of a cell as claimed.**

The specification disclosure does not recite or has given examples of the identified up or down regulated IBD genes or the probes generated from the genes identified or the micro arrays. The specification discloses that the libraries of nucleic acid probes (at least 5 genes refers to a library) for indexing the level of expression of one or more IBD genes. And the IBD probes will be isolated nucleic acids comprising a nucleotide sequence which hybridizes under stringent conditions to a sequence of table 1(e.g., see page 3). Further the specification discloses that the nucleic acid probes for indexing the level of expression of IBD genes are nucleic acid sequences (12-40 consecutive nucleic acids) correspond to the IBD gene set. Thus, the IBD gene set in Table 1 is not directly used in the claimed invention. Nucleic acid sequences identical or which correspond to the nucleic acid sequences of the IBD gene set in Table 1 has to be determined such that the identified nucleic acid sequences can be used as probes in the claimed method.

The claimed method depends upon identifying nucleic acid sequence probes after hybridizing with known IBD gene set, and prepare micro arrays using the identified probes and use the array in the claimed method. The specification does not disclose the nucleic acid sequences, which are identified after hybridizing with the known IBD gene set. Without knowing the probes (or nucleic acid sequences) it is impossible to practice the claimed method. Without the disclosure of the probes (or nucleic acid sequences) used in the claimed method, the specification description is hypothetical.

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The specification disclosure is narrative and based on hypothetical method. The specification does not include any working examples or experiments in which the genes involved in up- or down-regulated in intestinal tissue of patients are used in the method of determining phenotype or to assess a patient's risk of having or developing an inflammatory bowel disease. Thus, applicants are not in possession of the genes involved in the IBD.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Thus, it requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s).

In the present instance, the claimed invention contains no identifying characteristics regarding the probes used in the claimed method.

Additionally, the specification in absence of working examples is clearly not representative of the presently claimed invention.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 5-7 and 19-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alexander et al (Digestive Diseases and Sciences, Vol. 41, No. 4 (April 1996), pp 660-669) and Poulakkainen (G4358), and Prehn et al (G4355) (Gastroenterology, vol 114, No. 4, April 1998).

Alexander et al disclose a method to determine altered expression of protooncogenes (cell cycle related genes) in patients with inflammatory bowel disease (IBD). The reference assayed transcripts of 15 protooncogenes (refer to IBD genes) in colonic epithelial cells of IBD patients and controls (e.g., see abstract). The reference discloses that increased levels (refers to the differential expression of the instant claim) of soluble mediators (e.g. Leukotrienes, prostaglandins) of inflammation as well of the cells of immune system have been found to be present in the intestinal mucosa and submucosa of IBD patients (e.g., see page 660, last paragraph bridging first paragraph in page 661). The reference discloses expression of transcripts of eight growth factor receptor related genes in colonic epithelial cells of IBD patients and controls (i.e., see left column in page 661). The reference discloses that increased expression of PDGF-R- mRNA involved epithelium, compared to matched uninvolved epithelium, and the transcript level of this gene, as well three other growth factors was considerably higher in colonic epithelial cells of IBD patients (i.e., see page 661).

The reference discloses that prior to determining whether there were any differences between IBD samples and controls in their relative expression of protooncogene transcripts, it was necessary to determine the degree of expression of each of the genes in normal colon epithelial cells (i.e., see page 662, right column, section under results). The reference discloses that hybridization of radio labeled probes to slot blots of RNA extracted from normal epithelial cells of patients rejected for diverticulitis and sporadic cancer revealed that transcripts of five protooncogenes were abundant in these samples (refers to a method of selecting genes involved in IBD). The reference discloses that the level of expression of *c-fos* in the involved IBD samples was about twofold higher than in the uninvolved IBD samples (refers to instant claim 6).

The claimed invention differs from the prior art teachings by reciting differential expression of at least 5 genes, (or different number of genes as in claims 20-23) shown in table 1. Alexander et al teach the expression of protooncogenes in inflammatory bowel disease. Alexander et al teach a method to determine the differential expression of genes involved in IBD. The instant claim recites expression of at least five genes from table 1. However, the genes in the instant specification table 1 are not novel genes, and are well known for their role in IBD. Applicants in the specification disclose the Genbank accession numbers of the genes used in the claimed method. Thus, all the genes used in the claimed method are well known in the art. Puolakkainen et al (G4358) teach distinct expression profiles of stromelysin-s, collagenase and MMP-12 in intestinal ulcerations. Note that the crohn's disease (CD), ulcerative colitis (UC) are part of larger group of IBDs. And Prehn et al teach the role of TNF-alpha in CD, IL-18, IL-12, IL-10, IL-4. Thus, it would have been obvious to one skilled

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in the art at the time the invention to use all the known genes involved in IBD and use the genes (or probes) in array format to determine the IBD or pre-IBD phenotype. A person skilled in the art would have been motivated to use all the known genes or genetic markers involved in IBD in an array format to screen IBD cells, such that the efficiency of the method improves (i.e., more markers used the more different mechanisms involved in IBD are determined).

9. Claims 5-7 and 19-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dieckgraefe et al (Gastroenterology, vol 114, No. 4, April 1998) in view of specification disclosure.

Dieckgraefe et al disclose a method for identifying gene expressed in IBD. The reference have used GeneChip expression monitoring system to examine mucosal gene expression in ulcerative colitis, Crohns' colitis, and both in inflamed and non-inflamed non IBD specimens. The reference's aim was to identify gene markers differentially expressed in Crohns' disease and ulcerative colitis; identify genotype associated with disease subsets and characteristics. The reference in methods disclose RNA isolated from the mucosa of colonic reaction specimens was used to generate hybridization probes, and light directed solid-phase combinatorial chemistry was used to generate oligonucleotide probe array. The reference in results section discloses that dramatic changes were seen in the expression of wide range of genes, and genes were identified which appear to be specific markers for the specific diagnosis, disease activity and specific feature of histology. The reference clearly do not recite the genes or probes used in the method, however the reference disclosure that the genes involved in the ulcerative colitis and Crohn's disease from specimens of both inflamed and

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non-inflamed IBD specimens indicate that any IBD marker genes or probes can be used in the method.

The claimed invention differs from the prior art teachings by reciting determining expression of at least five genes (or more) from table 1. Dieckgraefe et al teach a method of identifying gene expression in IBD using Genechip technology. Dieckgraefe et al do not teach the genes in the table 1. However, as applicant's argue that the genes are well known in the art as markers of IBD (or involved in IBD). Thus a person skilled in the art would have motivated to use the method of Dieckgraefe et al and the known genes in determining the differential expressed genes in IBD. Applicants in the specification disclose the Genbank accession numbers of the genes used in the claimed method. Thus, all the genes used in the claimed method are well known in the art. Thus, a person skilled in the art at the time the invention was filed would have motivated to use the well known genes (all these genes are known to have a role in IBD) in the method taught by Dieckgraefe et al because Dieckgraefe et al teach the advantages of using Genechip technology in high through-put diagnostic assay.

Response to Arguments

10. Applicant's arguments filed on 11/14/03, regarding the written description rejection have been fully considered but they are not persuasive. Applicants argue that the specification discloses the nucleic acid probes useful in the claimed methods hybridizes under stringent conditions to a sequence shown in Table 1. Genebank accession numbers in the Table 1 correspond to the gene sequences, and further describing sequence identities and lengths of nucleic acid probes useful in the invention. Applicants arguments have been considered and are

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not persuasive, since the table 1 or (the only table in the specification starting at page 51) does not disclose the nucleic acid probe sequences or the length of the nucleic acid probes or the % homology of the probes. The specification nowhere sufficiently teach the probes used in the claimed method. Applicants further argue that the claimed method does not recite detection using probes in array format and can be practiced using a variety of techniques. However, applicant's arguments are irrelevant to the rejection of the instant claim, because applicants have not shown in possession of the probes used in the claimed method.

11. In view of applicant's amendments to the claims and the response filed on 11/14/03 the rejections under 35 U.S.C 112, second paragraph have been withdrawn.

12. Applicant's arguments filed 11/14/03, regarding the rejection of claims over Alexander et al are moot in view of new rejections.

13. Applicant's arguments with respect to claims 5-7, 19-29 over Dieckgraefe et al have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

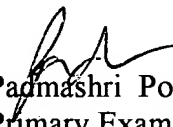
14. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Flex schedule and can be reached Monday through Friday between 7AM and 3.30 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

Pp
February 09, 2004.